

Fatal fungal infections resist newest class of drugs

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Fungi that cause severe infections in those with compromised immune systems are resisting the action of the latest group of antifungal drugs. Uncovering their strategies for doing this will lead to more effective treatments, says a scientist speaking at the Society for General Microbiology's Autumn Conference at the University of York.

<u>Candida albicans</u> is the most common hospital-acquired <u>fungal infection</u> and can cause illness by sticking to and colonizing plastic surfaces implanted in the body such as catheters, cardiac devices or prosthetic joints. From there the fungus can spread through the bloodstream to the major organs. While normally harmless to healthy individuals, *C. albicans* can cause fatal infections in immunocompromised people such as those suffering from cancer, trauma and <u>organ transplantation</u>.

Fungi such as *C. albicans* are covered in a sugar-rich outer layer (cell wall) that protects the fungus from the environment. The newest class of <u>antifungal drugs</u>, the echinocandins, targets the enzyme that makes one of the two key sugar polymers found in the cell wall, called beta-glucan. Scientists at the University of Aberdeen are investigating how *C. albicans* responds to echinocandins and have shown how the fungus is able to change the structure of its cell wall to render the drug ineffective.

Dr Carol Munro who is leading the research along with Professor Neil Gow explained, "If levels of drug are used that do not kill the fungus straight away, *C. albicans* responds by producing an excess of the other key cell wall sugar polymer, called chitin. <u>Fungal cells</u> displaying higher



levels of chitin can survive treatment with echinocandins, allowing infection to progress."

Echinocandins are given by IV injection and have a relatively broad spectrum of activity against most <u>Candida species</u>. The increasing number of reports of sporadic breakthrough infections in patients receiving echinocandin therapy is worrying, explained Dr Munro. "Echinocandins are used to treat Candida infections that may already be resistant to the azole group of antifungals. Healthcare specialists must be made aware of the potential problems and should keep up to date with the results of global surveillance programmes reported in the specialist literature."

The group's work will help improve treatment options for patients who experience antifungal failure. "Understanding the mechanisms of drug resistance will help us determine when it is appropriate to switch to a different drug regime. Our work so far suggests that the use of drugs that inhibit the production of chitin (if they were available), in combination with echinocandins, would improve treatment effectiveness for *Candida* infections," said Dr Munro. This work therefore, also impacts on the development of much needed novel antifungal therapies.

Provided by Society for General Microbiology

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